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## Interaction states by iterating maps in molecular biology

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### Introduction

Biological systems are consisted by hierarchy of many kinds of systems with very different time scalings each other. Sometimes this causes an important phenomena, namely random interaction in micro scale can form several patterns in macro. Here one wants to try to express them by using the dynamical systems of iterating maps.

In part I, we will describe which kinds of properties in micro scopic interaction systems might occur when one uses iteration of maps. Molecular interaction systems are equipped with various types of operations, for example switching of genes, various kinds of cycles including biological clocks, and mutations. We will describe how such phenomena might occur in the systems of iterations of maps.

This part mainly consists of explanation of biological phenomena by interpreting them into several properties of iteration of maps, which also includes suggestion of direction of mathematical formulation rigorously.

In part II, we will formulate micro interaction by use of composition of maps, which is used in [K2]. There we have a realization of some parts of the description in part I in a rigorous way. In particular we have studied how random micro interaction defined by this way can form several patterns in more macroscopic scales. In part II, we state shortly some results from [K2].

### I A description of interaction phenomena

#### 1 Feedback system

When proteins play roles in bio-mechanisms as molecules, like enzymes, their dynamics seem to hold both aspects, deterministic and non-deterministic behaviours. The former is because many proteins are polymers and whose dynamics apply classical mechanics. Quantum effect by electron enters into

the latter. In particular in chemical reaction, molecular oscillation plays a very important role. One important point is that these have very different time scalings mutually. Here one will try to represent *bio-interaction* systems by taking into account of these features.

Let  $f : [0, 1] \rightarrow [0, 1]$  be a map. In general structure of the range will be very complicated. A point  $x \in [0, 1]$  will represent a *state* of a molecule. An *oscillation* of  $x$  is the orbit:

$$\{f^n(x)\}_{n=0,1,\dots} = x, f(x), f^2(x), \dots$$

Dynamics of a molecule is a long-time behaviour of the oscillations. We are mainly interested in behaviour of states around period orbits:

$$P(n) = P(n)(f) = \{x \in [0, 1] : f^n(x) = x\}.$$

When a molecule is interacting with other molecules or is of phase transition, then its oscillation, or hybridization shows chaotic behaviour in quantum chemistry. An element  $x \in [0, 1]$  near the set  $P(n)$  will behave either stable or unstable manners. Unstable points will cause chaotic phenomena.  $x \in P(n)$  is regarded as a *high state*, if  $n$  is large. When  $x$  is a small periodic point, then it is in a low state.

In order to consider dynamics of molecules, here one uses simple differential equations including time parameter. This parameter corresponds to the large scaling compared with oscillations of molecules.

Now take a smooth function  $h : [0, 1] \rightarrow \mathbf{R}$  which could show gradient of energy functional at a state  $x \in [0, 1]$ . With respect to the time parameter, *feedback equation* for a single state is written as:

$$\dot{x} = -h(x).$$

This represents a large scale dynamics, and we need to take into account of small scale oscillations.

Molecules can change the states into very different quantum states. This is the *tunnel effect*. One way to express this phenomena is to use the energy potential surfaces by introducing extra parameter (e.g. complex coordinate).

One may construct  $h$  using the energy potential surfaces. On the plane  $[0, 1] \times \mathbf{R}$ , one plots a point  $(x, y)$  for each periodic point  $x \in [0, 1]$  with period  $y$  with respect to  $f$ . If one requires some Gaussian-like shapes for mountains on the plane, then one will need to change scale of  $x$  coordinate, say  $x \rightarrow x'$  which may be used as  $h(x) = x'$ .

## 2 Time scaling

In general time scalings are completely different between reaction velocity of enzymes and oscillation of the molecules. When genes are interacting, one cannot choose one state uniquely for each gene. Thus one is inevitably forced to take into account on all possible states, oscillations. If a molecule is in a state  $x$ , then one expresses all possible states of the molecule by iteration of  $f$  as:

$$f^k(x), \quad k \in \{0, 1, 2, \dots\}.$$

Let  $h : [0, 1] \mapsto \mathbf{R}$  be a function. In order to express a large scale dynamics, one will consider the following family of the equations:

$$\dot{x}^k(t) \equiv -h(x^k), \quad x^k(0) = f^k(x)$$

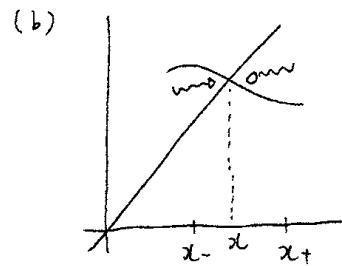
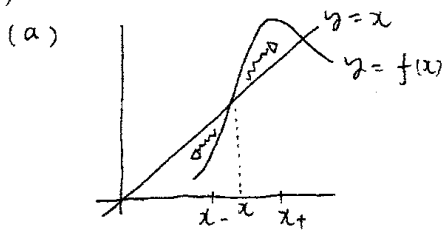
where  $x^k$  represents a variable. We will call the above equation as *feedback equation* for the oscillation. Iteration of the families of solutions:

$$\{f^l(x^k)(t)\}_{l,k}$$

will represent dynamics of the molecule. Let us put  $y_k(t) = \{f^l(x^k(t))\}_l$ . We will call  $y_k(t)$  as the *solution states*.

**2.B Simple patterns:** Let us consider dynamics of the above equations. Suppose  $x$  is a fixed point by  $f$ , and take a small  $\delta > 0$  and put  $x_{\pm} = x \pm \delta$ .

Let us consider two cases that its derivative satisfies (a)  $f'(x) > 1$  or (b)  $< 1$ . For (a), both  $x_{\pm}$  are unstable points, and for (b),  $x_{\pm}$  are stable points. Namely as  $k \rightarrow \infty$ ,  $f^k(x_{\pm})$  will be away from  $x$  for (a), and approach to  $x$  for (b).



There are two cases;

$$(1) \quad h(x) \geq 0 \quad \text{or} \quad (2) \quad h(x) \leq 0.$$

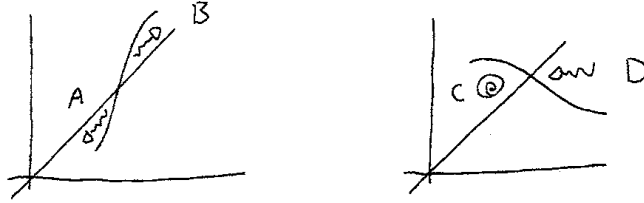
Let us consider the case (a). After a small time,  $x$  will move to  $x_-$  for (1) and  $x_+$  for (2). In both cases (1) and (2), their iterations  $f^k(x_{\pm})$  will move away from  $x$ . Since the effect of  $-h(x)$  also helps to move on the same direction, These cases of dynamics will be *strongly unstable*. In these cases, the molecule will move to another states.

Suppose (b) holds. Then  $x$  will move to  $x_{\pm}$  as above. Notice that the iterations  $f^k(x_{\pm})$  will both converge to  $x$  as  $k \rightarrow \infty$ . If (1) holds, then the effect of the dynamics will try to make  $x_-$  to move away from  $x$ , so the dynamics will be in an *equilibrium state*. If (2) holds, the dynamics will help to converge to  $x$ , and so it will be *strongly stable*. When two molecules are interacting in strongly stable states, then they will consist of a *polymer*.

For the case (b) and (2), we will say that *self-feedback* works.

We will gather these four patterns for the feed-back equation case in the following;  $x$  moves to:

$$\begin{cases} (A) & x_- \text{ (strongly unstable), } f'(x) > 1, \quad h(x) \geq 0, \\ (B) & x_+ \text{ (strongly unstable), } f'(x) > 1, \quad h(x) \leq 0, \\ (C) & x_- \text{ (equilibrium state), } f'(x) < 1, \quad h(x) \geq 0, \\ (D) & x_+ \text{ (strongly stable), } f'(x) < 1, \quad h(x) \leq 0. \end{cases} \quad (2.1)$$



Next let us consider the case that  $x$  is a periodic point, rather than a fixed one. For simplicity, we will assume that the period is 2,  $x < f(x)$  and there are no other periodic points in  $(x, f(x))$ .

At the beginning of time, the molecule is oscillating in  $\{x, f(x)\}$ . Unlike to the case of fixed points, here one needs to consider local behaviours of iteration both at  $x$  and  $f(x)$ . In this case, we have two differential equations:

$$\begin{aligned} \dot{x}^0(t) &\equiv -h(x^0), & x^0(0) &= x, \\ \dot{x}^1(t) &\equiv -h(x^1), & x^1(0) &= f(x). \end{aligned}$$

After a small time, the molecule also can choose any states  $\{x^0(t), x^1(t)\}$ . Molecular oscillation is quite random, and so within a small time, it will take any states in  $\{f^k(x^0(t)), f^k(x^1(t))\}_k$ .

If the case (C) hold at both  $x$  and  $f(x)$ , then the self-feedback does work for both  $x^0$  and  $x^1$ , and so the molecular states will stay near  $\{x, f(x)\}$ .

If (1) holds at both  $x$  and  $f(x)$ , then its states cannot stay near  $\{x, f(x)\}$ , and they will move near another periodic points along  $f^k(x^0(t))$  or  $f^k(x^1(t))$  randomly. There are another cases, like  $f^k(x^0(t))$  stay near  $x$  and  $f^k(x^1(t))$  will move to another states (for example (C) at  $x$  and (1) at  $f(x)$ , etc).

In these cases, after a small time the states may stay near  $x$ , or move to another randomly.

We will say that self-feedback works, if each solution state  $y_i(t)$ ,  $i = 0, 1$  stays near a periodic orbit. In that case the enzyme takes its states near the periodic orbit as the next time step.

We have described very simple patterns, but in general the orbits of states will be much more complicated, and may show chaotic behaviour.

### 3 Interaction

**3.A Simple interactions:** In our framework, a state of an enzyme  $A$  is expressed by an element  $x \in [0, 1]$  near  $P(n)$  for some  $n$ . Now let us take two proteins  $A_1$  and  $A_2$ , and suppose  $A_2$  acts on  $A_1$  as a *repressor* (*activator* resp.). Suppose that at a time  $t$  these are in states  $x_1$  and  $x_2$  respectively. Repressing (resp. activating) dynamics are expressed by differential equations as:

$$\dot{x}_1^k(t) = -h(x_2^k) \quad (\text{repressor}) \text{ or, } \dot{x}_1^k(t) = h(x_2^k) \quad (\text{activator}).$$

Combining with self-feedback, one can totally write the equations for the activator case as:

$$\begin{cases} \dot{x}_1^k(t) = h(x_2^k) - h(x_1^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = -h(x_2^k), & x_2^k(0) = f^k(x_2). \end{cases} \quad (3.1)$$

Let us consider the patterns of this dynamics as in the previous section. In this simple case, there are no interaction from  $A_1$  on  $A_2$ , and for the case of  $x_2$ , one can trace its behaviour as in the section 2. Let us take a fixed point  $x_1$ . The point is the sign of  $h(x_2^k) - h(x_1^k)$ . There are two cases:

$$(1) \quad h(x_2^k) - h(x_1^k) \geq 0, \quad (2) \quad h(x_2^k) - h(x_1^k) \leq 0.$$

If the molecule starts from  $x_1$ , then one may follow the dynamics of  $A_1$  by the same way as section 2. Let us put  $x_{\pm} = x_1 \pm \delta$ , and take another  $x_1 < x'_1 < x_+$ . suppose at the beginning,  $A_1$  has the state  $x'_1$ . Then we have the following diagram;  $x'_1$  moves to:

$$\begin{cases} x_+ \text{ (strongly unstable),} & f'(x_1) > 1, & h(x_2^k) - h(x_1^k) \geq 0, \\ x'_1 \text{ (equilibrium state),} & f'(x_1) > 1, & h(x_2^k) - h(x_1^k) \leq 0, \\ x'_1 \text{ (equilibrium state),} & f'(x_1) < 1, & h(x_2^k) - h(x_1^k) \geq 0, \\ x_1 \text{ (strongly stable),} & f'(x_1) < 1, & h(x_2^k) - h(x_1^k) \leq 0. \end{cases} \quad (3.2)$$

For example suppose  $f'(x_1) > 1$  and both  $h(x_2^k)$  and  $h(x_2^k) - h(x_1^k)$  are negative. Then as the quantity of  $A_2$  is gradually increasing, the state of  $A_1$  cannot stay near  $x_1$ . Namely  $A_1$  will change from an equilibrium state into a strongly unstable one.

One may consider the case when  $A_1$  starts at the state  $x_- < x_1'' < x_1$  by a parallel way.

Let  $y^1(t)$  and  $y^2(t)$  be the solution states respectively. If  $y^i(t)$  stay some periodic orbits  $p_1$  and  $p_2$  respectively, then we will say that this system is *stable*. Also in that case these enzymes take states near  $p_1$  and  $p_2$  respectively as the next time steps.

**3.B Intermediate time scale of interactions:** Let us consider systems between enzymes  $A_1$  and  $A_2$  which interact mutually as activators. Taking into account of self-feedback, one obtains an activating system on the large scale of time as:

$$\begin{cases} \dot{x}_1^k(t) = h(x_2^k) - h(x_1^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = h(x_1^k) - h(x_2^k), & x_2^k(0) = f^k(x_2). \end{cases} \quad (3.3)$$

By solving these equations, one obtains two sets of solutions  $\{x_1^k\}$  and  $\{x_2^k\}$ .

If one takes into account of the *order* to interact, then one needs to consider smaller time scale. For example first  $A_1$  acts on  $A_2$ , and after the effect of the interaction  $A_2$  becomes an activating state and then is able to act on  $A_1$  conversely, and so on.

There are two different initial directions of interactions:

$$A_1 \rightarrow A_2, \quad A_2 \rightarrow A_1.$$

For the first case, one starts from  $A_1$  and it interacts on  $A_2$ . Then  $A_2$  acts on  $A_1$ . They repeat to interact mutually. For the other case, one changes the roles of  $A_1$  and  $A_2$ . Let us consider the first case, and follow its procedure. First one solves the equation:

$$\dot{x}_1^k = -h(x_1^k), \quad x_1^k(0) = f^k(x_1).$$

Then using  $\{x_1^k\}$ , one solves another equations:

$$\dot{x}_2^k(t) = h(x_1^k) - h(x_2^k), \quad x_2^k(0) = f^k(x_2).$$

One considers another equations:

$$\dot{x}_{1,2}^k(t) = h(x_2^k) - h(x_{1,2}^k), \quad x_{1,2}^k(0) = f^k(x_1).$$

One iterates this process. Namely consider the equations:

$$\dot{x}_{2,2}^k(t) = h(x_{1,2}^k) - h(x_{2,2}^k), \quad x_{2,2}^k(0) = f^k(x_2).$$

Using  $\{x_{2,2}^k\}$ , again one solves the followings:

$$\dot{x}_{1,3}^k(t) = h(x_{2,2}^k) - h(x_{1,3}^k), \quad x_{1,3}^k(0) = f^k(0).$$

Successively iterating to solve the equations, one obtains families:

$$\{x_{1,m}^k\}, \quad \{x_{2,m}^k\}.$$

Let us recall that in the first paragraph of 3.B, we have  $\{x_1^k\}$  and  $\{x_2^k\}$ , families of solutions in the large scaling time. Now we will say that the original interaction system is *stable in smaller time scale*, if for each  $k$  and  $i = 1, 2$ , both  $x_{i,m}^k$  and  $x_i^k$  stay near the same periodic orbit for all sufficiently large  $m$ . We will denote the situation by  $\{x_{i,m}^k\}_k \sim \{x_i^k\}_k$  for large  $m$ .

Let us consider the converse path. If one starts from  $A_2$  to  $A_1$ , then the parallel argument will yield another families  $\{w_{1,m}^k, w_{2,m}^k\}$ . We will say that the original dynamical system with the initial states  $x_1$  and  $x_2$  is *cyclic*, if:

$$\{x_{1,m}^k\}_k \sim \{w_{1,m}^k\}_k, \quad \{x_{2,m}^k\}_k \sim \{w_{2,m}^k\}_k$$

hold for all sufficiently large  $m$ .

This is the simplest circuit of the interaction system. A little bit more general circuit will be as:

$$A_1 \rightarrow A_2 \rightarrow \dots A_N \rightarrow A_1.$$

One formulates stability for this system completely by the same way. One may start from  $A_2$ , and consider the following path:

$$A_2 \rightarrow A_3 \rightarrow \dots A_N \rightarrow A_1 \rightarrow A_2.$$

In this case also one obtains a notion of cyclicity.

## 4 Systems

Let us consider a system by mutually interacting enzymes:

$$\{A_1, \dots, A_N\}$$

with the initial states  $\{x_1, \dots, x_N\}$  respectively. One can consider various *routes* of interaction. In fact, for each *oriented signed graph* with self-loops



and with a subset of  $\{x_1, \dots, x_N\}$  as vertices, there associated with an interacting system. For example for a full graph (every pair of edges is connected), one obtains a family of the equations:

$$\begin{cases} \dot{x}_1^k(t) = -h(f^k(x_1)) + \sum_{j=2}^N \pm h(x_j^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = -h(f^k(x_2)) + \sum_{j \neq 2} \pm h(x_j^k), & x_2^k(0) = f^k(x_2), \\ \dots & \dots, \\ \dot{x}_N^k(t) = -h(f^k(x_N)) + \sum_{j \neq N} \pm h(x_j^k), & x_N^k(0) = f^k(x_N). \end{cases} \quad (4.1)$$

Let  $G$  be an oriented signed graph whose set of vertices is consisted by a subset of  $\{x_1, \dots, x_N\}$ . We will say that the set  $(f; x_1, \dots, x_N)$  is a *pre-interaction system*, and  $(f; x_1, \dots, x_N; G)$  is an *interaction system*. For an oriented signed graph, we will say it is an *interaction graph*.

Let  $(f; x_1, \dots, x_N; G)$  be a stable interaction system in the sense of 3.A. We will say that it is *stable under small perturbation*, if there exists  $\epsilon > 0$  such that for any  $(x'_1, \dots, x'_N)$  with  $|x_i - x'_i| < \epsilon$ , another interaction system  $(f; x'_1, \dots, x'_N; G)$  is also stable.

**4.B Cyclic system:** Let us consider a system consisted by  $N$  enzymes  $(A_1, \dots, A_N)$ . Suppose each  $A_i$  is being activated by  $A_{i-1}$ , and catalyzes on  $A_{i+1}$ , where we consider mod  $N$ . Each  $A_i$  takes a state  $x_+(i)$  when being silence, and  $z_-(i)$  when activating.

For example suppose there exists a pair  $x(i) < z(i)$  for each  $i$  such that both  $x(i)$  and  $z(i)$  are fixed points, there are no other periodic points between them and  $f(x) < x$  hold for  $x \in (x(i), z(i))$ .

We take  $x(i) < x_+(i) \ll z_-(i) < z(i)$ . The dynamics can be written as:

$$\dot{x}_i^k = -x_i^k + x_{i-1}^k.$$

Thus when  $A_{i-1}$  is in a low state, then  $A_i$  will also be in a low state and near  $x_+(i)$ . If the state of  $A_{i-1}$  is high and near  $z_-(i-1)$ , then the state of  $A_i$  will be also high and near  $z_-(i)$ .

This is a stable interaction system.

**4.C Cirrgadian rythms:** Let  $G$  be an oriented signed graph. We will say that  $G$  *lifts* periodically, if an infinite numbers of  $G$  can be connected periodically. We will denote the result by  $\tilde{G}$ .

Let  $(f; x_1, \dots, x_N; G)$  be a stable interaction system which lifts to also a stable periodic system  $(f; x_1, \dots, x_N; \tilde{G})$ .

We will say that  $x_m$  is a *clock gene*, if any of the interaction systems as  $(f; x_1, \dots, x_{m-1}, x_{m+1}, \dots, x_N; G')$  cannot lift stably.

## 5 Evolution

Let  $(f; x_1, \dots, x_N)$  be a pre-interaction system, and

$$\mathfrak{P} = \mathfrak{P}(f; x_1, \dots, x_N) = \{P_1, \dots, P_k\}$$

be a set of stable interaction graphs. Vertices of  $P_i$  are consisted by subsets of  $\{x_1, \dots, x_N\}$ . We will say that the set is *stable under small perturbation*, if there exists  $\epsilon > 0$  such that for any  $(x'_1, \dots, x'_N)$  with  $|x_i - x'_i| < \epsilon$ , another pre-interaction system  $(f; x'_1, \dots, x'_N)$  admits also the same set of the stable interaction graphs.

Recall that the *codon correspondence* is not one to one. For each amino acid, there associated with several codon triples. If a *mutation* does not change the corresponding amino acid, then it would not influence on the corresponding protein itself. When this type of mutation (called *mutation*) has occurred, the interaction system itself will not be influenced. It is known that this type of mutation occurs very often in a real life.

We will say that an interaction system  $(f; x'_1, \dots, x'_N; G')$  is an *apparent mutant* of  $(f; x_1, \dots, x_N; G)$ , if the corresponding sets of interaction graphs are the same,  $G = G'$ .

Let us regard that a set of interaction graphs represents a macroscopic system of a life. Let  $\mathfrak{P}_1$  and  $\mathfrak{P}_2$  be two sets of interaction graphs with respect to  $(f; x_1, \dots, x_N)$  and  $(f; y_1, \dots, y_N)$  respectively. We will say that  $\mathfrak{P}_1$  and  $\mathfrak{P}_2$  are mutually *close species*, if for any small  $\epsilon > 0$ , the following holds; there exists an interaction system  $(f; x'_1, \dots, x'_N; \mathfrak{P}_1)$  which is an apparent mutant to  $(f; x_1, \dots, x_N; \mathfrak{P}_1)$ , and another interaction system  $(f; x''_1, \dots, x''_N; \mathfrak{P}_2)$  with  $|x'_i - x''_i| < \epsilon$ , such that  $(f; x''_1, \dots, x''_N; \mathfrak{P}_2)$  is an apparent mutant to  $(f; y_1, \dots, y_N; \mathfrak{P}_2)$ .

**Example:** Let us consider two enzymes  $A_1$  and  $A_2$  and consider to obtain equilibrium systems. As before we consider a simple example. Suppose  $f$  has two fixed points  $x > x'$ , there are no other periodic points between them and  $s > f(s)$  hold for all  $s \in (x', x)$ . Let us consider the situation that  $A_2$  acts on  $A_1$  as an enhancer. Take  $x_+ = x + \delta$ , and consider a pre-interaction system  $(f; x_+, x_2)$  where  $x_2$  may be arbitrary. In order to be in an equilibrium state,  $A_2$  catalyzes as a repressor (section 2):

$$\begin{cases} \dot{x}_1^k(t) = -f^k(x_1) - x_2^k, & x_1^k(0) = f^k(x_+), \\ \dot{x}_2^k(t) = -f^k(x_2), & x_2^k(0) = f^k(x_2). \end{cases} \quad (5.1)$$

Now suppose a mutation occurs on  $A_1$  and suppose  $A_1$  has become to take its state as  $x_- = x - \delta$ . As far as  $A_2$  plays a role of repressor, the states of  $A_1$  will fall down into  $x'$ . After such process, if one wants to obtain an equilibrium state near  $x'$ ,  $A_2$  should catalyze as an activator.

In this case the sign of the edge between  $A_1$  and  $A_2$  changes.

**5.B Evolution dynamics by enhancers:** In some occasions, macroscopic evolution has occurred by mutation of enhancers. This shows that some macro phenomena can be understood by the strength of the activity of molecules.

Let  $\epsilon > 0$  be small, and let us take a simple pre-interaction system,  $(f; x_1, x_2)$  and two dynamics:

$$\begin{cases} \dot{x}_1^k(t) = -h(x_1^k) \pm h(x_2^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = -h(x_2^k), & x_2^k(0) = f^k(x_2). \end{cases} \quad (5.2)$$

$$\begin{cases} \dot{x}_1^k(t) = -h(x_1^k) \pm (1 + \epsilon)h(x_2^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = -h(x_2^k), & x_2^k(0) = f^k(x_2). \end{cases} \quad (5.3)$$

In both cases,  $x_2^k$  acts on  $x_1^k$  as an enhancer, but its strength are mutually different. Let  $\{x_1^k, x_2^k\}_k$  be the set of solutions for the second dynamics (5.3). Suppose a mutation occurs on  $x_2$  and changes it to  $x_3$ . Then one again considers the dynamics:

$$\begin{cases} \dot{x}_1^k(t) = -h(x_1^k) \pm h(x_3^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_3^k(t) = -h(x_3^k), & x_3^k(0) = f^k(x_3). \end{cases} \quad (5.4)$$

Let  $\{z_1^k, z_3^k\}_k$  be the set of the solutions for this dynamics. We will say that the evolution is induced by a *mutation of enhancers*, if the followings hold (3.B for  $\sim$ ):

$$\{x_1^k\}_k \sim \{z_1^k\}_k, \quad \{x_2^k\}_k \sim \{z_3^k\}_k.$$

**Example:** Let us choose two enzymes as in the example in 5.A, and consider the situation that  $A_2$  acts on  $A_1$  as an activator. Let us consider again to obtain equilibrium systems. In this case suppose  $f$  has two fixed points  $x < x'$ , there are no other periodic points between them and  $s < f(s)$  hold for all  $s \in (x, x')$ . Take  $x_+ = x + \delta$ , and consider an interaction system  $(f; x_+, x_2)$ :

$$\begin{cases} \dot{x}_1^k(t) = -x_1^k + x_2^k, & x_1^k(0) = f^k(x_+), \\ \dot{x}_2^k(t) = -x_2^k, & x_2^k(0) = f^k(x_2) \end{cases} \quad (5.5)$$

In order for this system to be in an equilibrium state, the inequality  $x_1^k > x_2^k$  should hold.

Suppose  $A_2$  begins activating on  $A_1$  more strongly. Let us change the notation of the variable by  $z_1^k$ :

$$\dot{z}_1^k(t) = -z_1^k + (1 + \epsilon)x_2^k > 0.$$

When the sign of the right hand side has changed, then  $z_1^k$  will increase and approach near  $x'$ . After some time, this will become an equilibrium state, since the value  $z_1^k$  will increase until near  $(1 + \epsilon)x_2^k$ .

**5.C Conservation of structure of proteins:** If *homology* of two sequences of genes are more than 30 percent, then one may guess these will share with the same *ancient*, and will have very similar protein structures or functions.

Some genes have mutually very different sequences, but the corresponding proteins have turned out to be very resemble each other. This was found by X-ray analysis, e.g., mioglobin and hemoglobin for some species.

In an interaction network, functions of proteins will tend to be conserved, but within such conservation, sequences might be changeable frequently. Let us choose a family of periodic points  $\{p_1, \dots, p_N\}$ . Then we put:

$$P(\{p_1, \dots, p_N\}) = \{G : (f; x_1, \dots, x_N; G) : \\ \text{the solution states } \{f^l(x_i^k)\}_{k,l} \text{ stay near } p_i\}.$$

## 6 Bio-functional quantity

**6.A Liapunov exponent:** Let  $f : [0, 1] \mapsto [0, 1]$  be a  $C^1$  map. Then at  $x \in [0, 1]$ , the Liapunov exponent  $\lambda(x)$  is defined by:

$$\begin{aligned} \lambda(x) &= \limsup_{n \rightarrow \infty} \frac{1}{n} \log(|(f^n)'(x)|) \\ &= \limsup_{n \rightarrow \infty} \frac{1}{n} \sum_{j=0}^{n-1} \log(|f'(f^j(x))|). \end{aligned}$$

When this number is negative, then  $x$  is stable. Namely  $\lambda$  satisfies some continuity in some sense, and any orbits near  $x$  will approach to the one of  $x$ . If  $\lambda(x) > 0$ , then the situation will drastically change. It will be far from to be continuous, and orbits will be sensitively influenced by the initial points near  $x$ . In fact one has the Taylor expansion:

$$|f^n(x + \delta) - f^n(x)| \sim |(f^n)'(x)\delta| \sim |\delta|L(x)^n, \quad L(x) = \exp(\lambda(x)).$$

$L(x)$  satisfies  $1 >$  or  $< 1$  according to the signs of  $\lambda(x)$ .

**6.B Simple cases:** Let us consider the simplest case of interaction system, and try to obtain its *bio-functional quantity*.

Let  $(f; x)$  be the single feed back system which is followed by the dynamics:

$$\dot{x}^k(t) = -x^k, \quad x^k(0) = f^k(x).$$

Then one defines a parametrized bio-functional quantity by:

$$\lambda(\alpha, x) = \limsup_{n \rightarrow \infty} \frac{1}{n} [\log(|(f^n)'(x)|) + \alpha \log f^n(x)], \quad \alpha > 0.$$

In general the inequality holds,  $\lambda(\alpha, x) \leq \lambda(x)$ .

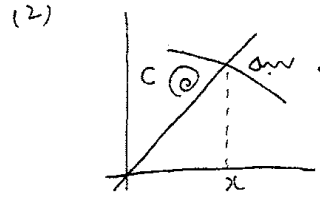
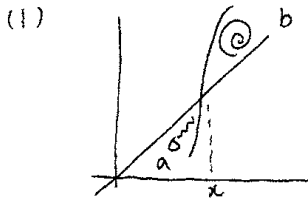
One may have a picture for this number as follows. Let  $x$  be a fixed point of  $f$ .

(1) If  $|f'(x)| > 1$ , then:

- (a)  $x_- = x - \delta$  will be strongly unstable with respect to  $x$ ,
- (b)  $x_+ = x + \delta$  will be an equilibrium point,

(2) If  $f'(x) < 1$ , then:

- (c)  $x_- = x - \delta$  will be an equilibrium point,
- (d)  $x_+ = x + \delta$  will be strongly stable with respect to  $x$ .



The above situation is expressed by the bio-functional quantity:

$$\lambda(d) < \lambda(c), \lambda(b) < \lambda(a).$$

We will say that  $\lambda(\alpha, x)$  in (b) or (c) are *equilibrium invariants*.

**6.C Interaction system by two enzymes:** For interaction systems consisted by more than two enzymes, one can obtain also bio-functional quantities. For simplicity, suppose  $h$  is a map between intervals  $h : [0, 1] \mapsto [0, 1]$ , and consider a system with feedback plus enhanser:

$$\begin{cases} \dot{x}_1^k(t) = \pm h(x_2^k) - h(x_1^k), & x_1^k(0) = f^k(x_1), \\ \dot{x}_2^k(t) = -h(x_2^k), & x_2^k(0) = f^k(x_2). \end{cases} \quad (6.1)$$

In this case one obtains parametrized bio-functional quantities by:

$$\begin{aligned}\lambda(\alpha, x_1) &= \\ \limsup_{n \rightarrow \infty} \frac{1}{n} [\log(|(f^n)'(x_1)|) - \alpha(\pm \log h(f^n(x_2)) - \log h(f^n(x_1)))], \\ \lambda(\beta, x_2) &= \limsup_{n \rightarrow \infty} \frac{1}{n} [\log(|(f^n)'(x_2)|) + \beta \log h(f^n(x_2))].\end{aligned}$$

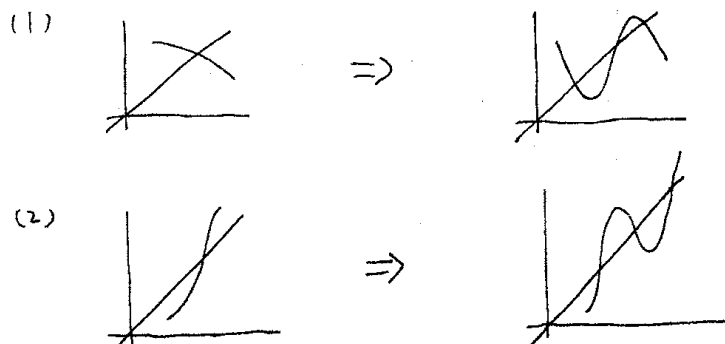
For more general stable systems  $(f; x_1, \dots, x_N; G)$ , one obtains the bio-functional invariants:

$$(\lambda(\alpha_1, x_1), \dots, \lambda(\alpha_N, x_N))$$

by the completely analogous way.

## 7 Iterating functions with parameter

Let  $f_s : [0, 1] \mapsto [0, 1]$  be a family of maps. When the Schwartz derivatives of  $f_s$  are all negative, like the Logistic maps, then the behaviour of periodic points are well studied. Suppose  $x$  is a fixed point of  $f_{s_0}^n$ . Then as the parameter  $s$  moves from  $s_0$  to  $s_1 = s_0 + \delta$ ,  $f_s$  looks like as:



For (1), let us consider the single feedback system in 6.B. During the movement of the parameter,  $x_- = x - \delta$  drastically falls down into another periodic point  $x_-^1$ .  $x_+ = x + \delta$  is strongly stable at  $s_0$ , and changes into an equilibrium state at  $s_1$ .

**9.B Doubling genes:** Let  $f_s : [0, 1] \rightarrow [0, 1]$  be a parametrized map, and suppose periodic orbits have *pitchfork bifurcation*, e.g., the logistic map  $f_s(x) = sx(1 - x)$ .

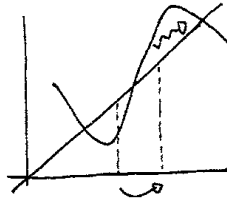
In *neutral theory* in evolution, bifurcation of species is explained by mutation by *doubling genes*. If a doubling of a gene occurs, then in order to keep the system, it will be enough if one of them plays the role of the original function. So the other may be free to mutate if the result would not affect the system itself.

In our setting, one may have a picture of doubling genes by regarding  $s$  as the *evolutional time parameter*.

Let us take an embedding of two oriented signed graphs  $G \subset H$ . Let  $(f_s; x_1, \dots, x_N; G)$  be an interaction system, and let us move the parameter  $s$ . At the point  $s^1 = s + \delta$  of bifurcation, let us double some states, say  $x_i$ :

$$(f_{s^1}; x_1, x_2, \dots, x_{i-1}, x_i, x_i, x_{i+1}, x_{i+2}, \dots, x_N; G)$$

where a vertex of  $G$  corresponds to the first of  $x_i$ 's. Suppose  $x_i$  is in an equilibrium state before bifurcation. One may perturb the other  $x_i$  slightly at  $s^1$  so that it will move to another periodic orbit.



As a result one will obtain another interaction system at  $s_+^1 = s^1 + \delta$ :

$$(f_{s_+^1}; x_1, x_2, \dots, x_{i-1}, x_i, x'_i, x_{i+1}, x_{i+2}, \dots, x_N; H)$$

where a vertex of  $H \setminus G$  is consisted by  $x'_i$ .

Let  $s = s^0, s^1, \dots$  be the ordered set of bifurcation points.  $\lim s^i = s^\infty$  is known as the *Feigenbaum constant* for the logistic map. At each time  $s^i$ , one may choose an evolutionized interaction system:

$$\begin{aligned} \mathcal{I}_i &= (f_{s^i}; x_1^i, \dots, x_N^i; H_i), \\ H_0 &= G \subset H_1 \subset \dots \subset H_i \subset \dots \end{aligned}$$

The family  $\{\mathcal{I}_i\}_i$  represents an evolution of a system by doubling genes.

## 8 Switching of genes

Enzymes play roles of *switching* in a biological systems. Let us choose an enzyme in a system. The system contains two states, namely when the enzyme is activating and catalyzing the other molecules, and another is when being silence. Let us represent this situation in our setting.

Let  $(A_1, \dots, A_N)$  be the set of molecules which consists of an interaction system. When  $A_N$  is being silence, and in a state  $z$ , its interaction system may be expressed by:

$$(f; x_1, \dots, x_N, z; G)$$

where  $G$  does not contain  $z$  as a vertex.

Suppose  $A_{N-1}$  works as a co-enzyme on  $A_N$  and  $A_N$  begins activating. Then the system will change as:

$$(f; x'_1, \dots, x'_N, z'; H)$$

where  $H$  contains  $z'$  and may be very different from  $G$ .

A simple description of switching was given in 3.A.

**8.B Systems by binary enhancers:** Let  $(A_1, \dots, A_N)$  be a system consisted by enzymes. Each  $A_i$  is catalyzed by another enzyme  $A'_i \in \{A_1, \dots, A_N\}$ , and it takes two states  $x_i$  or  $z_i$  according to whether it is catalyzed by  $A'_i$  or not. Suppose each  $A_i$  catalyzes another two enzymes  $B_i$  or  $C_i \in \{A_1, \dots, A_N\}$  when  $A_i$  is in states  $x_i$  or  $z_i$  respectively. Namely  $A_i$  changes the partners to catalyze whether it is activating or not. Then we will say that  $A_i$  is a *binary enhancer* and works as a *switching*.

$$A'_i \rightarrow A_i \begin{array}{l} \xrightarrow{x_i} B_i \\ \xrightarrow{z_i} C_i \end{array}$$

**Example:** Let us consider a system by  $(A_1, A_2, A_3)$ , and suppose  $A_2$  takes two states between the interval  $(x(2), z(2))$  where  $x(2)$  and  $z(2)$  are both fixed points, there are no other periodic points and  $f(x) < x$  hold in the interval.  $A_3$  takes two states between  $(x(3), z(3))$  which has the same properties except that  $f(x) > x$  hold in the interval.  $A_1$  takes two states,  $x_1$  and  $z_1$  satisfying  $h(x_1) \ll 0$  and  $h(z_1) \gg 0$ .

Let us consider a pre-interaction system  $(f; x, x_+(2), z_-(3))$  where  $x$  may be arbitrary.  $A_2$  and  $A_3$  admit the dynamics:

$$\dot{x}^k(i) = -x^k(i) + h(x_1), \quad i = 2, 3.$$

When  $x = x_1$ , then  $A_1$  catalyzes only on  $A_2$ , and when  $x = z_1$ , it does only on  $A_3$ .

## II Interaction by composition of maps

Below we will show one realization of interaction of maps by way of compositions which has described in part I. Under such formulation, we have studied several analytic properties and relations with other fields in [K2].

Passing through small scaling  $n$  in iterations of maps  $\{h^n\}$  to a larger one  $t$  in another iteration  $\{\Phi(x)^t(\bar{k})\}_t$ , flow of the interaction maps, we obtain a pattern formation from micro interactions.



## 9 Interaction of maps

Let us take two interval maps:

$$f, g : [0, 1] \rightarrow [0, 1]$$

and consider their iterations:

$$O_1(x) = \{f^k(x)\}_{k=0,1,\dots}, \quad O_2(x) = \{g^k(x)\}_{k=0,1,\dots}.$$

We call them as the *oscillatins* ([K2]).

Let us have a symbolic dynamics  $X_2$  by two alphabets  $\{0, 1\}$ . Then for each element  $\bar{k} = (k_0, k_1, \dots) \in X_2$ , we will associate a family of maps:

$$\{h^k(x)\}_{k=0,1,\dots}$$

as follows. Let us put:

$$d_i(x) = \begin{cases} f(x) & i = 0, \\ g(x) & i = 1. \end{cases}$$

Then we define  $h^k$  by:

$$h^k(x) \equiv d_k \circ d_{k-1} \circ \dots \circ d_0(x).$$

Let:

$$\pi : [0, 1] \rightarrow \{0, 1\}$$

be a measurable map. For example one may choose  $\pi([0, \frac{1}{2})) \equiv 0$  and  $\pi([\frac{1}{2}, 1]) \equiv 1$ . Then for each  $x \in [0, 1]$ , one can compose the interaction with  $\pi$ . Thus one obtains another element for a.e.  $x$ :

$$\pi((h^1(x), h^1(x), \dots)) \equiv (\pi \circ h^0(x), \pi \circ h^1(x), \dots) \in X_2.$$

We call:

$$\Phi(x, f, g) : X_2 \rightarrow X_2$$

by  $\Phi(x, f, g)(\bar{k}) \equiv \pi((h^0(x), h^1(x), \dots))$  as the *interaction map*.

We call  $x \in [0, 1]$  a *regular point*, if  $\Phi(x)$  is a homeomorphism. Let:

$$G = G(f, g) = \{\Phi(x) : x \in [0, 1], \text{ regular}\} \subset \text{Aut } X_2$$

be a group generated by  $\Phi(x)$  for all regular points  $x$ .

One can generalize the construction of  $\Phi(x)$  by using more than two maps. In fact using four interval maps  $f, g$  and  $\alpha, \beta$ , one can obtain the corresponding interaction map  $\Phi(x)$ , and  $G(f, g, \alpha, \beta)$ .

**Proposition 9.1 (K2)** *There is a family of interval maps  $(f, g, \alpha, \beta)$  such that the corresponding  $G \subset \text{Aut } X_2$  is isomorphic to the lamplighter group  $\oplus_{\mathbb{Z}} \mathbb{Z} / \mathbb{Z}_2 \rtimes \mathbb{Z}$ .*

In particular for  $f, g, f', g'$  above, the group  $G$  acts on  $\partial X_2$  ergodically.

By dividing  $[0, 1]$  into  $L + 1$  subintervals, one can immediately generalize the above construction. Thus using family of maps, one obtains interaction maps  $\Phi(x) : X_{L+1} \rightarrow X_{L+1}$ .

A flow of  $\bar{k} \in X_{L+1}$  is an orbit set:

$$\{\Phi(x)^t(\bar{k})\}_{t=0}^{\infty} \subset \text{Aut } X_2.$$

The *ultra-discrete Lotka Vorterra equation* is given by the following families of equations (see [HT]):

$$v_n^{t+1} - v_n^t = \max(0, v_{n+1}^t - L) - \max(0, v_{n-1}^{t+1} - L).$$

It is known that they have solitons in solutions.

**Proposition 9.2 (K2)** *There is a family of smooth maps  $\{f_{i,j}\}_{i,j=0,\dots,L}$  so that the flow of the corresponding interaction map gives solutions of the Lotka Vortarra cell automaton.*

## References

- [CG] A. CARBONE AND M. GROMOV, *Mathematical slices of molecular biology*, IHES preprint, (2001).
- [HT] R. HIROTA AND D. TAKAHASHI, *Discrete and ultradiscrete systems*, in Japanese, Kyoritsu shuppan, (2003).
- [K1] T. KATO, *Operator dynamics in molecular biology*, IHES preprint (2001).
- [K2] T. KATO, *Interacting maps, symbolic dynamics and automorphisms in molecular biology*, Kyoto University preprint (2004).
- [UK1,2] K. UENO AND T. KATO EDS., *Introduction to molecular biology for mathematicians*, in Japanese, (2003, 2004).

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